DETAILED ACTION

Applicants' arguments, filed 3/1/2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 1, 28 and 55 have been cancelled and replaced with claims 140-159. Newly submitted independent claim 140 corresponds to previously rejected claim 1, newly submitted independent claim 147 corresponds to previously rejected claim 28 and newly submitted independent claim 140 corresponds to previously rejected claim 55.

Election of Species

In response to the Office Action sent 9/31/2009, applicant cancelled all claims and filed a new claim set. The new claims, received 3/1/2010, necessitate a new election.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

The following species election is required:

a) *Linking molecule:* Such as recited by claims 141-144.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner: all claims are generic as to the above recited species.

Restriction is proper because as discussed in the Office Action dated 8/31/2009 and herein incorporated by reference, Green (U.S. 6,267,957) teaches polylysine as a linking molecule for an active such as hyaluronic acid (col. 13, lines 12-17).

A phone call was placed to Mr. Edward Gates with regard to the species election. An oral election polylysine was made. Mr. Gates stated that a polylysine conjugate read on claims 140, 141, 143-148, 150-155, and 157-159.

Accordingly, **Claims 142, 149 and 156** are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicants are reminded that upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Claim Rejections - 35 USC § 112 – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 140, 141, 143-148, 150-155 and 157-159 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See, e.g., In re Wilder, 22 USPQ 369, 372-3 (Fed. Cir. 1984). (Holding that a claim was not adequately described because the specification did 'little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.')

Mere indistinct terms (such as a conjugate of hyaluronic acid and a linking molecule that is a "substrate of translutaminase", "derivative of lysine" of "derivatives of glutamine" used herein), however, may not suffice to meet the written description requirement. This is particularly true when a compound is claimed in purely functional terms. See Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886 (CAFC 2004) at 1892, stating:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning

> of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

Conversely, a description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. See Univ. of Calf. V. Eli Lilly, 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under Section 112, ¶ 1, by showing the enablement of a representative number of species within the genus.

A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. *If the genus has substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus.* See MPEP 2163. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any *combination of such identifying characteristics that distinguish the claimed invention from other materials* and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. MPEP 2163.

Here, the specification does not provide a reasonably representative disclosure of useful lysine derivatives or glutamine derivatives generally, a potentially huge genus inclusive of many different compounds having widely divergent structures and functions.

Specifically, the specification does not appear to disclose and derivatives, but rather states that derivatives include analogs and salts. This description is not viewed as being reasonably representative of the genus in its claimed scope because no readily apparent combination of identifying characteristics is provided, other than the disclosure of those specific species as examples of the claimed genus.

Note, Applicants have amended the claims to define the linking molecule as at least two contiguous aliphatic amines or two contiguous carboxamides, wherein the amines are lysine or a derivative of lysine, and wherein the carboxamides are glutamine or a derivatives of glutamine.

Examiner disagrees. While the new limitation recites additional structure, it is unclear if the linking molecule require the lysine or glutamine in specific locations or how far derived the linking molecule may be and still be a substrate of transglutaminase.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 147, 148, 150 and 151 stand rejected under 35 U.S.C. 102(b) as being anticipated by Asayama (Synthesis of Novel Polyampholyte Comb Type Copolymers Consisting of a Poly(L-lysine) Backbone and Hyaluronic Acid Side Chains for a DNA carrier, Bioconjugate Chem. Vol. 9, pp. 476-481, 1998 – See IDS dated 12/10/2007).

First, Applicants argue that claim 147 (formerly claim 28) requires that the linking molecule is uncomplexed, while the prior art does not teach a composition which is

uncomplexed with DNA. Second, Applicants argue that the prior art does not teach a composition which for treating dryness and containing an effective amount of the conjugates of the invention.

Examiner disagrees. First, Asayma does teach a composition wherein the linking molecule is uncomplexed with DNA (See Asayma at p. 477, scheme 1).

Second, the claims are drawn to a composition, so the intended use of treating dryness is immaterial to the patentability of the claim. Further, any amount of the HA-graft-PLLA that has any effect is sufficient to meet the "effective amount" claim limitation, given the claims are directed to a composition and any recitation of use is deemed an intended use and not liming of the composition. Here, the HA-graft-PLLA was demonstrated to affect the turbidity of the solution (p.477, turbidity measurement) and therefore has an "effective amount" to affect turbidity.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., effective amount to treat dry eye) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 147, 148, 150-155, 157 and 158 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Green (U.S. 6,267,957).

First, Applicants assert that Green does not teach that the tissue sealant for mechanically sealing wounds has any utility in the eye or the use of an eye dropper bottle. Second, Applicants assert that Green does not disclose a pharmaceutical composition, and thus Green does not suggest (i) a pharmaceutical preparation for treating dryness, (ii) a solution of a hyaluronic acid-polylysine conjugate, and (iii) an effective amount of the conjugate for treating dryness. Third, Applicants argue that Green does not teach a solution for treating dry eye or an effective amount of hyaluronic acid and a linking molecule for treating dry eye.

Examiner disagrees. First, Green teaches the composition may be in the form of an eye dropping solution, ophthalmic ointment, or contact lens solution (¶18). Thus, it is clear the composition can be used for the eye and in the form of an eye dropper. It would have been obvious to administer an eye dropping solution from an eye dropper bottle.

Second, it is noted that the claims are drawn to a composition, specifically a pharmaceutical composition. The word "pharmaceutical" simply requires the use of the composition be suitable for pharmaceutical application. Note, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Here, the composition taught by Green is a

composition comprising a pharmaceutical agent (col. 13, lines 26-27) which uses a hyaluronic acid conjugate to seal wounds (col. 13, lines 12-20), i.e. a pharmaceutical application. Thus, the composition taught by Green is a pharmaceutical composition which may contain a hyaluronic acid-polylysine conjugate. Though it does not appear that the instant claims recite the limitation that the conjugate formulation be in the form of a "solution", it is noted that Green teaches the composition may be in the form of an eye dropper or contact lens solution (¶18).

Note, treating dry eye is not recited in the claims, and even if it were, as discussed above, the recitation would be viewed as an intended use. Where the composition has other uses, the patentability of the subject matter is based on the composition, not the intended use.

Claims 140, 141, 143-148, 150-155, and 157-159 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Green (U.S. 6,267,957) in view of Cantoro (U.S. 5,770,628)

First, Applicants assert that because Green teaches a tissue sealant is used to mechanically seal wounds, Green does not render obvious the instantly recited invention. Second, Applicants assert that Green does not disclose a pharmaceutical composition, and thus Green does not suggest (i) a pharmaceutical preparation for treating dryness, (ii) a solution of a hyaluronic acid-polylysine conjugate, and (iii) an effective amount of the conjugate for treating dryness. Third, Applicants assert Green does not teach that the tissue sealant for mechanically sealing wounds has any utility in

the eye or the use of an eye dropper bottle. Fourth, Applicants assert that Green does not teach that tissue sealants are useful in the eye and Cantoro does not teach that free hyaluronic acid would have any application in the arena of tissue sealants.

Examiner disagrees. First, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, the prior art teaching meets the recited claim limitation. Here, Green teaches a composition comprising a hyaluronic acid conjugate wherein polylysine may be the linking molecule (col. 13, lines 12-20). Since the claims are drawn to a composition and the prior art the recited elements, the claims is rendered obvious regardless of the label the prior art uses to describe the function of the component (i.e. tissue sealant). The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. MPEP §2112.

Second, it is noted that the claims are drawn to a composition or a pharmaceutical composition. Green teaches a composition comprising a pharmaceutical agent (col. 13, lines 26-27). Further, Green uses a hyaluronic acid conjugate to seal wounds (col. 13, lines 12-20), which is a pharmaceutical application. Thus, the composition taught by Green is a pharmaceutical composition which may contain a hyaluronic acid-polylysine conjugate. Though it does not appear that the instant claims require the conjugate to be in the form of a "solution", it is noted that Cantoro teaches

an ophthalmic solution (e.g. col. 6, lines 14-24). Treating dry eye is an intended use of the composition (see above for intended use discussion).

Third, with regard to claim 154 and its dependants, Green teaches that when used in vivo, the agents are attached to body tissue, with a particular important body tissue being the surface of the eye (col. 7, lines 23-33). Thus, it would have been obvious to one of ordinary skill in the art to formulate the active ingredient into an ophthalmic composition in order to deliver the active to the particularly important tissue on the surface of the eye. It would have also been obvious to place the ophthalmic composition into a eye-dropper bottle for traditional application to the surface of the eye.

Fourth, in formulating the active ingredient of Green for administration to the eye, it would have been obvious to combine the active ingredient into a solution which is particularly suitable for ophthalmic administration. Thus, it would have been obvious to combine the active ingredient of Green, which is taught to be attached to the tissues on the surface of the eye, with a composition which is particularly suitable for ophthalmic delivery of an active, such as the solutions taught by Cantoro. Further, it would have been obvious to adjust the amount of free hyaluronic acid present in order to obtain a solution having the desired viscosity, given that Cantoro teaches hyaluronic acid acts as a thickener, which would affect the resulting viscosity.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ADAM MILLIGAN whose telephone number is (571)270-7674. The examiner can normally be reached on M-F 9:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fred Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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